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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/688,076	10/13/2000	Philip A. Beachy	JHUC-P01-016	8453

28120 7590 06/23/2003  
ROPES & GRAY LLP  
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BOSTON, MA 02110-2624

EXAMINER

YOUNG, JOSEPHINE

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 06/23/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/688,076

Applicant(s)

BEACHY, PHILIP A.

Examiner

Josephine Young

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-42 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

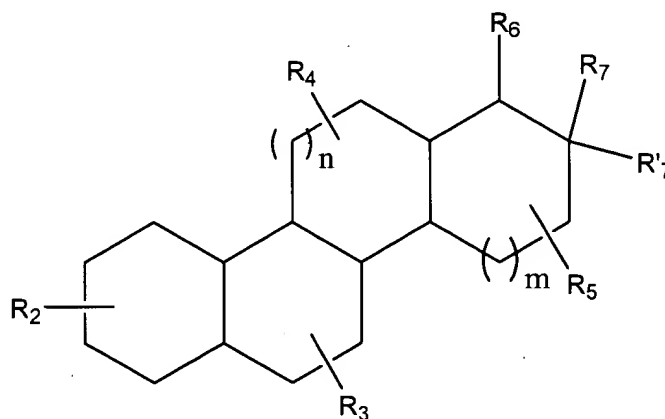
## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_ 6) ☐ Other:

**DETAILED ACTION*****Election/Restrictions***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-4, 5-6, 20 and 42, drawn to compounds of the formula (A), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:



(A)

wherein at least one of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> is a sugar; and

R<sub>6</sub> and R<sub>7</sub> are taken together to form a substituted or unsubstituted ring or polycycle that includes a tertiary amine in the atoms that make up the ring, and compositions with such compounds, classified in class 536, subclass 4.1<sup>+</sup>, 5, 6, 6.1, 6.2.

- II. Claims 1-4, 5-6, 7-10, 20 and 42, drawn to compounds of the formula (A), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof: wherein, at least one of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> is a sugar; and R<sub>7</sub> and R'<sub>7</sub> are taken together to form a substituted or unsubstituted ring or polycycle that includes a

tertiary amine in the atoms that make up the ring, classified in class 536, subclass 4.1<sup>+</sup>, 5, 6, 6.1, 6.2.

- III. Claims 5-6, 7-10 and 20, drawn to compounds of the formula (A), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof: wherein, at least one of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> is a sugar; and R<sub>7</sub> is independently a monocyclic or polycyclic group that includes a tertiary amine in the atoms that make up the ring that is linked to the core structure via an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, an ether or an amine linkage, classified in class 536, subclass 4.1<sup>+</sup>, 5, 6, 6.1, 6.2.
- IV. Claims 1-4, 5-6, 20 and 42, drawn to compounds of the formula (A), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof: wherein, none of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> is a sugar; and R<sub>6</sub> and R<sub>7</sub> are taken together to form a ring or polycycle that includes a tertiary amine in the atoms that make up the ring, classified in class 552, subclass 502<sup>+</sup>, 509<sup>+</sup>, 510, 514.
- V. Claims 1-4, 5-6, 7-10, 20 and 42, drawn to compounds of the formula (A), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof: wherein, none of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> is a sugar; and R<sub>7</sub> and R'<sub>7</sub> are taken together to form a substituted or unsubstituted ring or polycycle that includes a tertiary amine in the atoms that make up the ring, classified in class 552, subclass 502<sup>+</sup>, 509<sup>+</sup>, 508.
- VI. Claims 5-6, 7-10 and 20, drawn to compounds of the formula (A), or unsaturated forms thereof and/or seco-, nor- or homo-derivatives thereof:

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wherein, none of R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> is a sugar; and R<sub>7</sub> is independently a monocyclic or polycyclic group that includes a tertiary amine in the atoms that make up the ring that is linked to the core structure via an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, an ether or an amine linkage, classified in class 552, subclass 502<sup>+</sup>, 509<sup>+</sup>.

- VII. Claims 11-19, drawn to methods for treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, using compounds of Group I, classified in class 514, subclass 25, 26, 27, 28, 32, 33, 34, 35.
- VIII. Claims 11-19, drawn to methods for treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, using compounds of Group II, classified in class 514, subclass 25, 26, 27, 28, 32, 33, 34, 35.
- IX. Claims 11-19, drawn to methods for treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, using compounds of Group III, classified in class 514, subclass 25, 26, 27, 28, 32, 33, 34, 35.
- X. Claims 11-19, drawn to methods for treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development

of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, using compounds of Group IV, classified in class 514, subclass 167, 169, 170, 172, 176, 177, 178, 179, 180, 181, 182.

- XI. Claims 11-19, drawn to methods for treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, using compounds of Group V, classified in class 514, subclass 167, 169, 170, 172, 173, 176, 177, 178, 179, 180, 181, 182
- XII. Claims 11-19, drawn to methods for treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, using compounds of Group VI, classified in class 514, subclass 167, 169, 170, 172, 176, 177, 178, 179, 180, 181, 182.
- XIII. Claims 21-24, 25-26 and 31-41, drawn to methods for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype using compounds of Group I, classified in class 514, subclass 25, 26, 27, 28, 32, 33, 34, 35.
- XIV. Claims 21-24, 25-26, 27-30 and 31-41, drawn to methods for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype using compounds of Group II, classified in class 514, subclass 25, 26, 27, 28, 32, 33, 34, 35.

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- XV. Claims 25-26, 27-30 and 31-41, drawn to methods for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype using compounds of Group III, classified in class 514, subclass 25, 26, 27, 28, 32, 33, 34, 35.
- XVI. Claims 21-24, 25-26 and 31-41, drawn to methods for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype using compounds of Group IV, classified in class 514, subclass 167, 169, 170, 172, 176, 177, 178, 179, 180, 181, 182.
- XVII. Claims 21-24, 25-26, 27-30 and 31-41, drawn to methods for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype using compounds of Group V, classified in class 514, subclass 167, 169, 170, 172, 173, 176, 177, 178, 179, 180, 181, 182.
- XVIII. Claims 25-26, 27-30 and 31-41, drawn to methods for inhibiting *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype using compounds of Group VI, classified in class 514, subclass 167, 169, 170, 172, 176, 177, 178, 179, 180, 181, 182.

Claims 1-4 and 42 link Groups I, II, IV and V, and will be examined together with the Group that is elected as it pertains to the elected invention. Claims 7-10 link Groups II, III, V and VI, and will be examined together with the Group that is elected as it pertains to the elected invention. Claims 5, 6 and 20 link Groups I-VI and will be examined with the Group that is

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elected as it pertains to the elected invention. Claims 11-19 link Groups VII-XII and will be examined together with the Group that is elected as it pertains to the elected invention. Claims 21-24 link Groups XIII, XIV, XVI and XVII and will be examined together with the Group that is elected as it pertains to the elected invention. Claims 27-30 link Groups XIV, XV, XVII and XVIII and will be examined together with the Group that is elected as it pertains to the elected invention. Claims 25, 26 and 31-41 link Groups XIII-XVIII and will be examined together with the Group that is elected as it pertains to the elected invention.

The inventions are distinct, each from the other because of the following reasons:

Groups I-III are unrelated to Groups IV-VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed to compounds with patentably distinct functional groups. The compounds of Groups I-III are directed to steroid derivatives that are linked to a sugar moiety, while the compounds of Groups IV-VI do not have a sugar moiety. The compounds are deemed patentably distinct and there is nothing on this record to show them to be obvious variants. Therefore, the compounds/compositions of one do not render obvious the compounds/compositions of the other.

Groups I/IV are unrelated to Groups II/V, which are unrelated to Groups III/VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed to compounds



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with patentably distinct functional groups. The compounds of Groups I/IV are directed to steroid derivatives fused to a cyclic or polycyclic ring system, while the compounds of Groups II/V are directed to spiro derivatives of steroid, and the compounds of Groups III/VI are directed to steroid derivatives that are simply linked to a cyclic or polycyclic ring system. The compounds are deemed patentably distinct and there is nothing on this record to show them to be obvious variants. Therefore, the compounds/compositions of one do not render obvious the compounds/compositions of another.

Should applicant traverse on the ground that the groups are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Groups I-VI are related to Groups VII-XII as product and process of use. Similarly, Groups I-VI are related to Groups XIII-XVIII as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different process, namely the products can be used in the methods of Groups VII-XII or the materially different methods of Groups XIII-XVIII.

Groups VII-XII and Groups XIII-XVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of

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operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed patentably distinct methods with different effects. The methods of Groups VII-XII are directed to treating basal cell carcinoma, regulating differentiation or proliferation of a cell, controlling the growth or development of pancreatic tissue, treating medullablastoma, or treating a hyperproliferative disorder, while the methods of Groups XIII-XVIII are directed to inhibiting of *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype. The methods of one do not render obvious the methods of the other. Simply because methods for the treatment of a disorder or in regulating cell proliferation/growth conceivably could be mediated by inhibiting of *hedgehog* signaling or counteracting a *ptc* loss-of function phenotype or a *smoothened* gain-of-function phenotype, does not necessarily mean that the methods are restricted to such limitation.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, restriction for examination purposes as indicated is proper. A reference for one group could not reasonably be expected to be a reference for another. Further, searching all of the inventions constitutes a burdensome search, as a thorough search comprises a search of foreign patents and non-patent literature, as well as the appropriate U.S. patent classifications. To search the eighteen independent and distinct inventions, set forth supra, would indeed impose an undue burden upon the examiner in charge of this application.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even if the requirement is traversed (37 CFR 1.143).

If one of Groups I-VI are elected, Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. This application contains claims directed to the following patentably distinct species of the claimed invention:

- 
- The diagram shows a polycyclic chemical structure consisting of three fused six-membered rings on the left and a chain of two more six-membered rings on the right. The leftmost ring has a substituent  $R_2$  on its left side. The middle ring has a substituent  $R_3$  on its bottom side. The chain of two rings on the right has a substituent  $R_4$  on the top of the first ring, a substituent  $R_5$  on the bottom of the second ring, a substituent  $R_6$  on the top of the second ring, a substituent  $R_7$  on the top of the third ring, and a substituent  $R'7$  on the right side of the third ring. The chain of two rings is indicated by a bracket with a subscript  $n$  and a bracket with a subscript  $m$ .

(A)

- (B) a seco-derivative thereof;
- (C) a nor-derivative thereof; or
- (D) a homo-derivative thereof;

AND

wherein in each distinct species

- $n$  is either 0, 1 or 2;
- $m$  is either 0, 1 or 2;
- $R_6, R_7$  and  $R_7$  are distinct in that

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For Groups I and IV:

- $R_6$  and  $R_7$  are taken together to form a substituted or unsubstituted monocyclic ring that includes at least one tertiary amine in the atoms that make up the ring;
- $R_6$  and  $R_7$  are taken together to form a substituted or unsubstituted contiguous bicyclic ring that includes only one tertiary amine in the atoms that make up the ring, such that the tertiary amine is in the ring directly attached to the core structure;
- $R_6$  and  $R_7$  are taken together to form a substituted or unsubstituted contiguous bicyclic ring that includes only one tertiary amine in the atoms that make up the ring, such that the tertiary amine is not in the ring directly attached to the core structure; or
- $R_6$  and  $R_7$  are taken together to form a substituted or unsubstituted polycyclic ring with more than two contiguous rings that includes at least one tertiary amine in the atoms that make up the ring;

For Groups II and V:

- $R_7$  and  $R'_7$  are taken together to form a substituted or unsubstituted monocyclic ring that includes at least one tertiary amine in the atoms that make up the ring;
- $R_7$  and  $R'_7$  are taken together to form a substituted or unsubstituted contiguous bicyclic ring that includes only one tertiary amine in the

atoms that make up the ring, such that the tertiary amine is in the ring directly attached to the core structure;

- $R_7$  and  $R'_7$  are taken together to form a substituted or unsubstituted contiguous bicyclic ring that includes only one tertiary amine in the atoms that make up the ring, such that the tertiary amine is not in the ring directly attached to the core structure; or
- $R_7$  and  $R'_7$  are taken together to form a substituted or unsubstituted polycyclic ring with more than two contiguous rings that includes at least one tertiary amine in the atoms that make up the ring;

For Groups III and VI:

- $R_7$  is a substituted or unsubstituted monocyclic ring that includes at least one tertiary amine in the atoms that make up the ring that is linked to the core structure via an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, an ether or an amine linkage;
- $R_7$  is a substituted or unsubstituted contiguous bicyclic ring that is linked to the core structure via an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, an ether or an amine linkage, wherein the bicyclic ring includes only one tertiary amine in the atoms that make up the ring, and the tertiary amine is in the ring directly attached to the linker;
- $R_7$  is a substituted or unsubstituted contiguous bicyclic ring bicyclic ring that is linked to the core structure via an alkyl, an aminoalkyl, a carboxyl, an ester, an amide, an ether or an amine linkage, wherein the

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bicyclic ring includes only one tertiary amine in the atoms that make up the ring, and the tertiary amine is not in the ring directly attached to the linker; or

- R<sub>7</sub> is a substituted or unsubstituted polycyclic ring with more than two contiguous rings that includes at least one tertiary amine in the atoms that make up the ring.

Claims 1-10, 20 and 42 are generic to a plurality of disclosed patentably distinct species.

If one of Groups VII-XVIII are elected, Applicant is further required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. This application contains claims directed to patentably distinct species of the claimed invention, namely a patentably distinct methods using a distinct species as set forth supra.

Claims 11-19 and 21-41 are generic to a plurality of disclosed patentably distinct species.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the

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limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Josephine Young whose telephone number is (703) 605-1201. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

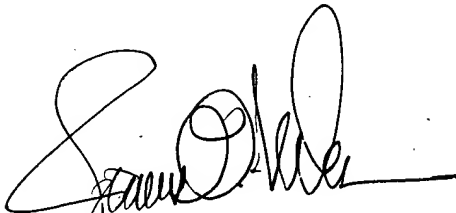
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (703) 308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JY

June 18, 2003



**JAMES O. WILSON**  
**SUPERVISORY PATENT EXAMINER**  
**TECHNOLOGY CENTER 1600**